ient cases should receive large doses of the hypnotics of which veronal is by far the best, whisky should be given regularly, and ergot administered at frequent intervals either by intramuscular injection or by mouth. Such medication should be discontinued gradually and only after all signs of restlessness and tremor have disappeared. The delirious patient should receive veronal in moderate doses—all other hypnotics and especially morphine and hyoscine should be withheld. Ergot should be given as in the incipient cases. So far as the delirious patients are concerned, our data do not give conclusive evidence whether or not whisky should be regularly employed.

THE CAUSE AND RELIEF OF PAIN IN DUODENAL ULCER.[1]

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The first mention in medical literature of duodenal ulcer is the report of two cases determined post mortem by Mr. Travers[2] in 1817. The second record is that by an American physician, Irvine, of Philadelphia; but it is to John Abercrombie,[3] a Scotch physician, that we must ascribe the priority of noticing the phenomenon that in disease of the duodenum food is taken with relish; that the first stage of indigestion is not interfered with, and that the pain begins about the time the food is leaving the stomach, namely, two to four hours after meals. This was in 1830.

It was not until 1887 that this symptom complex was reëstablished by Bucquoy,[4] who made the first symptomatic diagnosis which was confirmed at autopsy; the intervening fifty-seven years, containing only records of 143 cases collected from the pathologists and general hospital services where death had ensued from perforation, although in 1852, Wunderlich[5] mentions a case of death from perforation, in which it is stated that ulcer of the duodenum was suspected previously.

Codivilla,[6] an Italian surgeon, was the inaugurator of operative interference in cases of chronic non-perforated ulcer of the duodenum, when he demonstrated the efficacy of a gastro-enterostomy in this condition on March 22, 1893, and again on May 5, 1898.

[1] Read before the American Gastro-Enterological Association, April, 1911.

[2] Medico-Chir. Trans., London, viii, 232.

[3] Path. and Pract. Research of Dis. of the Stomach., Edinburgh, 1830, pp. 103, etc.

[4] Arch. gén. de méd., 1 to 398 et seq.

[5] Handbuch der Path. und Therap., 111 to 175.

[6] Sei Casi Gastroenterost Sperimentale. Mem. Orig. Firenza, 1893, pp. 406 to 421, and Contrib. alla chirug. gastrica., Bologne, 1898.

At first we were in the transition period between the epochs of surgery based on anatomy and that grounded on pathology, which latter has only been elaborated since Virchow, after the middle of the nineteenth century, brought forward his observations.

Now a new era has opened. Surgery based on physiology and its developments may be included within the past decade. It is to offer a contribution to this beginning epoch that I wish to present the following observations:

I have had the opportunity of examining personally previous to operation one hundred cases on whom an operation later by Dr. William Mayo confirmed the diagnosis of duodenal ulcer. The privilege of reporting the results of my study of these has been given me by the operator. In the present paper I wish to consider only those clinical points relevant to the time element of the occurrence of the pain, the method employed to relieve it, the promptness of its relief, and the degree of total acidity of the gastric juice.

The average time of the onset of epigastric distress in this series of consecutive cases, was between three and four hours after meals. Almost without exception the ingestion of any substance, water, alkalies, milk, cracker, beer, and even acids, caused the pain to stop immediately. Probably the diagnostic point of greatest significance that can be considered in relation to this phenomenon is the observation elicited from the patient that he usually goes to bed with some form of food or liquid beside him, as he knows that he will be awakened at a definite time and can only get to sleep again by taking a mouthful or two of the substance, which he has found from experience, will give him immediate relief, and, as briefly indicated above, his fancies may lead him to partake of the most bizarre things. So regular and unfailing are these occurrences that the term "clocksetters" has been applied to them, and, from that single word we should be able to make a correct diagnosis in possibly 90 per cent. of the cases presenting this symptom.

I have made complete pre-operative stomach analyses of all of these cases, and find that the average total acidity is 77, and determined that in approximately 70 per cent. there was a hypersecretion of this hyperacid juice. This fact is further confirmed by the subjective history that in nearly all cases the patients complain of sour, acrid, bitter, or burning eructations of a mouthful or two of stomach contents between meals, which, as they express it, "sets their teeth on edge;" and, indeed, it is so concentrated, that in many instances it has been corrosive in its action on the teeth, giving strong confirmatory evidence in the diagnosis of this condition.

As has been so plainly demonstrated by Edkins and Tweedy,[7] the production of gastric juice subsequent to the ingestion of a meal is after a time effected through the agency of the gastric hormone obtained from the pyloric mucosa, and in order to complete the preparation of a moderate mass the hydrochloric acid must be secreted in very considerable quantity; in fact, a much greater amount than is recoverable during the first hour. This conclusion is easily demonstrated by an analysis of a complex meal, if it be extracted during the third hour, or just as it is about to pass into the duodenum, when the acidity will be found to average between one and two hundred, or even higher.

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[7] Proc. Royal Soc., London, 1908, lxxx, 529.

It may then be considered even more than an inference that after the food has left the stomach entirely there is still an outpouring of hydrochloric acid, and in cases of duodenal ulcer this would seem to be greater in amount and concentration than is ordinarily the case—if I have been correct in my interpretation of the stomach analyses. This would seem to place the inferential conclusions that the pain was caused by the irritation of the ulcer by hydrochloric acid on a fairly firm chemical as well as clinical basis.

One other factor must be taken into consideration, namely, may not the pain be caused by spasm of the pylorus? This is by some accepted as the explanation. As bearing upon the possibility of this being the cause, the following observations should be carfeully considered:

If pyloric spasm was the etiological factor, the pain would be irregular in its onset; if food had any effect, it would be to increase the discomfort, rather than diminish it. In muscular spasm of the gastric outlet the distress is more indefinite, of less intensity, of shorter duration than that found in typical duodenal ulcer, and its radiation, if any, is downward toward the umbilicus, a phenomenon so characteristic of appendicular gastralgia, which *is* pylorospasm. Further, I have not seen demonstrated at operation very many instances of this peculiar unmistakable contraction of the pylorus in cases of duodenal ulcer, while it is perfectly demonstrable in the large majority of instances when the gastric discomfort emanates from the appendix or gall bladder. Finally, the two peculiar types of epigastric distress are occasionally found in the same patient, at the same time, two distinct subjective sensations. It will frequently be described as a steady burning, accompanied by a grinding, boring, irregular pain, and on taking food or drink the former is relieved, while the latter is temporarily unaltered.

If these hypotheses are correct, then the most plausible explanation for the control of the pain by the ingestion of food, etc., would be that this secretion was in some manner neutralized. To determine what this agent was, the following experiments were carried out for the purpose of ascertaining more definitely the physical and chemical properties of the duodenal secretion, if, indeed, there was any such fluid, and what effect reflex stimulation, from placing food in the stomach, would have on it. Ten adult dogs, averaging between twelve and fifteen pounds, were taken, and the following operative procedure was done on each (see figure):

1. Ligature of the pylorus.
2. Ligature of the duct of Wirsung.
3. Ligature of the duct of Santorini.
4. Ligature of the common bile duct.
5. Gastro-enterostomy 30 cm. from pylorus.
6. Cholecystostomy.
7. Ligature of the duodenum 15 cm. from pylorus.
8. Duodenostomy.

By these procedures it resulted that no extraneous secretion could enter the duodenum, while the secretion of the duodenum proper was prevented from escaping into the intestine below. By the final duodenostomy the recovery of the pure duodenal secretion was provided for.

In every instance the postoperative course was uneventful until between the fiftieth and sixtieth hours, when all the dogs died a "physiological death," due to the exclusion of the duodenal secretion from the remainder of the intestinal canal, as has been so perfectly demonstrated lately by Matthews,[8] and which was previously intimated by Maury.[9]

Twenty-six analyses were made, in some instances two, in others as many as five, of the secretion gathered from the duodenostomy tube. These showed an average alkalinity of 77, being titrated against an $\frac{N}{10}$ H_2SO_4 solution, using methyl orange as an indicator.

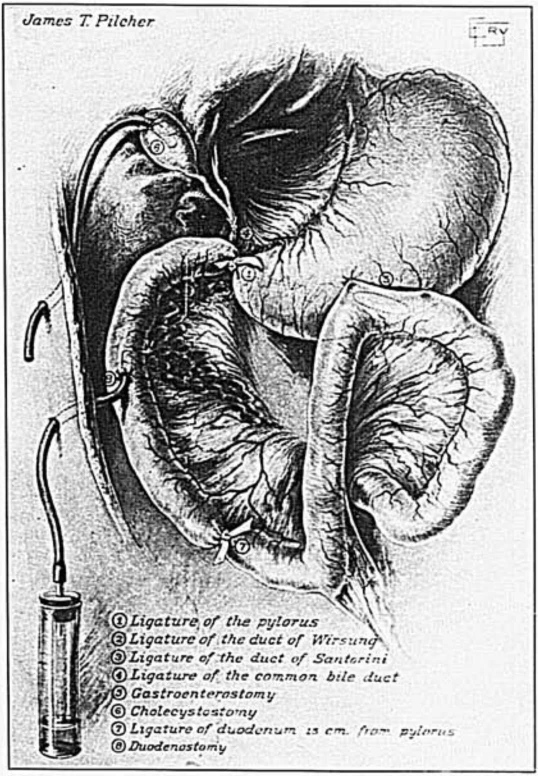
The duodenal secretion was obtained in every instance entirely free from pancreatic juice and bile, and in many of the specimens there was no mucus. The duodenal secretion thus obtained is of a light straw color, very slightly turbid (due to lymphocytes), is practically odorless, but decomposes very rapidly. It has a constant specific gravity of between 1006 and 1009 by weight, and is secreted on a starving stomach in quantities averaging between three and four hundred cubic centimetres, every twenty-four hours, it has practically negative digestive properties.

After determining what these factors were for each dog, without any stimulation or food or water, these elements were introduced to see what effect they might have on this secretion. In two instances the dogs were allowed to smell well-cooked meat, with the result that the secretion was markedly stimulated, *i. e.*, previous to experiment they were secreting 10 c.c. per hour; two minutes after smelling meat, 13 c.c. spurted out of the tube in one instance, in the other, about 5 c.c. was gathered within four minutes.

[8] Jour. Amer. Med. Assoc., 1910, lv, 293.

[9] Amer. Journ. Med. Sci., 1909, cxxxvii, 725.

Water was given at regular intervals (the dogs drinking with avidity, when allowed), and in *every* instance they secreted as much within five minutes as they had during the preceding hour, and if allowed to drink at will continued an increased secretion all day.


James T. Pilcher
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① Ligature of the pylorus
② Ligature of the duct of Wirsung
③ Ligature of the duct of Santorini
④ Ligature of the common bile duct
⑤ Gastroenterostomy
⑥ Cholecystostomy
⑦ Ligature of duodenum 15 cm. from pylorus
⑧ Duodenostomy

Illustrating the method devised to obtain pure duodenal secretion. The operative procedures should be undertaken in the order indicated by the numerals.

Strong beef tea was next introduced through a stomach tube, being retained usually about five minutes before it was regurgitated, during which time the duodenal secretion was more markedly stimulated than in either of the preceding series, and continued so for some time after having vomited the liquid. They refused in every instance to eat any food, so I was unable to make any other observations which would have been of interest.

This excess of secretion was of slightly lower alkalinity and one or two points lower in specific gravity, but for all practical purposes identical with that secreted previously. That it was stimulated through nerve reflexes hardly admits of question, as the duodenum was imperviously constricted at the pylorus and proximal to the gastro-enterostomy. That it was a pure secretion from the duodenal mucosa is evident, owing to the fact that the bile and pancreatic ducts were all ligated off securely. That it was not a transudation of the serum or lymph is indicated, because of its having a radically different specific gravity from any other known body fluid.

The absolute evidences of its stimulation being effected through the ingestion of any substance, and even through psychical reflexes, and its chemical properties, are too pertinent to lead us to believe that we are dealing with a mere coincidence. The cause of death in these dogs and the pathology of the organs in each case coincide strikingly with that noticed in human beings under similar circumstances. Some facts observed bearing upon the cause of death in cases in which the duodenum is involved I hope to have the opportunity of presenting at some later date.

From a study of the above, however, I feel justified in concluding that:

A. The cause of pain in duodenal ulcer is the hydrochloric acid contained in the gastric juice coming in contact with the ulcerated surface after it has passed into the duodenum. This conclusion is based on the following observations: (1) Ulcer of the duodenum reflexly excites a hyperacidity of the gastric juice; (2) the maximum amount of secretion of hydrochloric acid in the stomach is due to a direct chemical action (hormones) and is at its height from one to four hours after meals; (3) it passes into the duodenum as hydrochloric acid, there being no food for four hours after meals for it to work upon; and (4) it does not excite a flow of the duodenal juice directly, and is not neutralized by the small amount present.

B. The relief of pain in duodenal ulcer follows the ingestion of any substance into the stomach, and is due to a reflex stimulation of the duodenal secretion which neutralizes the acid gastric juice. This conclusion is based on the following facts already demonstrated in the above experiments: (1) Food taken into the stomach excites at once a reflex secretion in the duodenum; (2) the duodenal secretion is alkaline in approximately the same degree as the gastric juice is acid; and (3) this secretion is of sufficient quantity and concentration to neutralize the hydrochloric acid of the gastric juice.

These experiments were undertaken in the Hull Laboratories at the University of Chicago, under the direction and with the cooperation of Dr. S. A. Matthews.

THE COMPLEMENT-FIXATION TEST IN THE DIAGNOSIS OF GONOCOCCIC INFECTIONS.[1]

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To Müller and Oppenheim,[2] in 1906, belongs the credit of first applying the complement-fixation test to the study of the serum of a patient having gonorrhœal arthritis. This serum gave a positive reaction, and the serum of a patient suffering from disease not gonorrhœal gave a negative reaction, thus proving that gonorrhœal serum contains a specific antibody for the gonococcus. Further data were published by Bruck[3] later in 1906, and by Meakins,[4] Vannod,[5] and Wollstein,[6] in 1907. Teague and Torrey[7] also published a report in 1907 confirming the fact that all antigonococcic sera have the power to bind complement; but when several different strains of gonococci are used, strain "A" only reacts strongly with the serum from a rabbit immunized with strain "A;" and strain "B" only with the serum of a rabbit immunized with strain "B," and so on, which would seem to prove Torrey's contention that there are several different types of gonococci. An exhaustive report, including the study of a number of human and immunized rabbit sera, was published by T. Watabiki[8] in January, 1910, in which he confirmed the work of the previous investigators in its essential points.

During the last few months we have applied the complement-fixation test to a total of 324 human sera. These sera were taken

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[1] Read at a meeting of the New York Academy of Medicine, Section on Medicine, October 18, 1910.

[2] Wien. klin. Woch., 1906, No. 19, p. 894.

[3] Deut. med. Woch., 1906, No. 70, p. 36.

[4] Johns Hopkins Hosp. Bull., 1907, No. 18, p. 255.

[5] Zntrlbl. f. Bakter., 1907, No. 44, p. 10.

[6] Jour. Exper. Med., 1907, No. 9, p. 588.

[7] Jour. Med. Res., 1907, No. 17, p. 223.

[8] Jour. Inf. Dis., 1910, No. 7, p. 159.